

Abstract No. ye521

## **Design of an Amphiphilic Di-Helix and its Vectorial Orientation at the Air-Water Interface**

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Beamline(s): X22B

**Introduction:** Alpha-helical bundles can provide a structural framework for binding specific prosthetic groups at selected locations within the structure of an artificial peptide thereby designed to mimic a number of functions exhibited by biological proteins, including vectorial electron transfer. The first family of these artificial peptides was based on amphipathic di-helices (each helix possessing two faces, each composed of either nonpolar or polar residues, extending over the entire length of the helix) which self-assembled in aqueous solution to form four-helix bundles with a polar exterior and nonpolar interior and thought to be of *anti* (or antiparallel) topology[1]. In order to realize any potential device applications of these designed artificial peptides, it is necessary to vectorially orient an ensemble of such peptides, for example at an interface. In prior work, the di-helices were rendered amphiphilic via the covalent attachment of a C16 hydrocarbon chain to their amino terminus[2]. Electron density profiles derived from specular X-ray reflectivity showed that these amphiphilic di-helices could be vectorially-oriented at an air-water interface in a Langmuir monolayer at relatively high surface pressures, either in pure form or in binary mixtures with phospholipids, with their helical axes normal to the interface[3]. Any function exhibited by the peptide's prosthetic groups, e.g., vectorial electron transfer, would then necessarily occur in the aqueous phase, namely on one side of the air-water interface. In this work, each  $\alpha$ -helix of the di-helix is again designed to be amphipathic with one face composed of polar residues and the other composed of nonpolar residues. However, the primary sequence was designed such that if the nonpolar faces of each amphipathic helix were apposed in the di-helix over the first 1-28 residues of each helix, the polar faces would be apposed over the last fourteen residues 29-42. Here, the polar faces were composed of equal numbers of positively and negatively charged residues at neutral pH.

**Methods and Materials:** Monolayers were spread in a custom-built Langmuir trough mounted on the sample stage of the Liquid Surface Spectrometer of X22B and x-ray specular reflectivity data were collected as described elsewhere[3].

**Results and Conclusions:** Electron density profiles derived from specular x-ray reflectivity have shown that these di-helices vectorially orient at the air-water interface in Langmuir monolayers of the pure peptide only at relatively high surface pressure, while they orient at significantly lower surface pressures in binary mixtures with a diacyl phospholipid, presumably due to the insertion of the hydrophobic surface of the di-helix into the hydrocarbon chain layer of the phospholipid monolayer. Such amphiphilic di-helices allow for the positioning of prosthetic groups on either side of the air-water interface thereby allowing, for example, vectorial electron transfer across the interface.

**Acknowledgments:** This research supported by the NIH under grants GM33525, GM41048 and GM55876 and by the MRSEC program of the NSF under Award No. DMR96-32598. The National Synchrotron Light Source is supported by the U. S. Department of Energy under Contract No. DE-AC02-76CH00016.

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